Oral Presentations

ALLOGENEIC

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RISKS AND OUTCOMES OF IDIOPATHIC PNEUMONIA SYNDROME AFTER ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION: THE INTENSITY OF THE CONDITIONING REGIMEN OUTWEIGHS THE EFFECT OF ACUTE GRAFT-VERSUS-HOST DISEASE

Fukuda, T.; Hackman, R.C.; Guthrie, K.A.; Carter, R.A.; Sandmaier, B.M.; Davis, C.; Martin, P.J.; Storb, R.F.; Madtes, D.K. Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA.

Background: Idiopathic pneumonia syndrome (IPS) is one of the major causes of mortality after allogeneic hematopoietic stem cell transplantation (HCT). Here, we investigated the incidence, risk factors and outcomes of IPS after myeloablative compared to nonmyeloablative allogeneic HCT. **Methods:**We retrospectively analyzed data from patients who underwent allogeneic myeloablative (Conventional group; n=926) or non-myeloablative (NST group; n=183) HCT from related or unrelated donors at FHCRC between 12/1997 and 12/2001. IPS was diagnosed during the first 120 days after transplant, based on NHLBI criteria including 1) multilobar infiltrates identified by CXR or CT scan, 2) symptoms/signs of pneumonia and evidence of abnormal physiology, and 3) absence of active lower respiratory tract infection. Survival was defined as alive 30 days after hospital discharge. **Results:**Patient characteristics and clinical course after IPS of the 2 groups are summarized in the Table. Multivariate analysis demonstrated that NST was associated with a significantly decreased risk of IPS (HR 0.24, p=0.001), while age greater than 40 years and grades 3-4 acute GVHD were associated with significantly increased risks (HR 1.8, p=0.009 and HR 3.4, p=0.001, respectively). Survival of IPS patients to 30 days past discharge was 25% after either NST or conventional HCT. IPS patients who required mechanical ventilation (n=50) had a 2% survival while patients who did not require mechanical ventilation (n=31) had a 61% survival (p=0.001). The presence of renal failure at IPS onset (serum creatinine ∝2 mg/dl) was associated with an increased probability for death before or within 30 days of hospital discharge (OR 14, p=0.023) in a multiple logistic regression model. **Conclusion:**Recipients of NST have a significantly decreased risk of IPS compared to those given myeloablative conditioning despite greater patient age and similar incidence of severe acute GVHD. These findings suggest that lung damage from myeloablative conditioning plays a crucial role in the development of IPS after transplant and that acute GVHD alone is insufficient to cause IPS. IPS is associated with a high mortality rate despite aggressive support when mechanical ventilation is required or renal failure is present.

Patient Characteristics	Conventional (n=926)	NST (n=183)	p-value
Median age (years)	40	53	<0.001
Acute GVHD grades 3-4	27%	21%	n.s.
Incidence of IPS (days 0-120)	8.3%	2.2%	0.002
Clinical Course after IPS	**Conventional (n=77)**	**NST (n=4)**	
Median time to IPS onset after transplant (days)	22 (range 4-106)	16 (range 7-34)	
Mechanical ventilation (MV) required	62%	50%	
Median time to MV after IPS (days) (n=50)	1 (range 0-57)	2 (range 0-3)	
Survival to 30 days after hospital discharge	25%	25%	
Median time to death after IPS (days) (n=70)	14 (range 1-979)	15 (range 4-279)	

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TRAFFICKING OF EX VIVO EXPANDED DONOR DERIVED DENDRITIC CELLS AFTER ALLOGENEIC BMT

Schimmelpfennig, C.H.[1]; Tarner, I.H.[2]; Schulz, S.[4]; McBride, J.M.[2]; Baker, J.[1]; Fathman, C.G.[2]; Contag, C.H.[3]; Negrin, R.S.[1] 1. Stanford University Medical Center, Dpt. of Medicine, Div. of BMT, Stanford, CA; 2. Dpt. of Medicine, Div. of Immunology and Rheumatology, Stanford, CA; 3. Dpt. of Pediatrics, Div. of Neonatal and Developmental Medicine, Stanford, CA; 4. Dpt. of Microbiology and Immunology, Div. of Infectious Diseases, Stanford, CA.

Introduction: Little is known about survival and trafficking of *ex vivo* expanded DCs after adoptive transfer in animals. We investigated the trafficking patterns of allogeneic DCs transduced to express green fluorescence protein (gfp) and luciferase (luc) (gfp/luc$^+$ DCs) in mice that had received allogeneic BMT. Methods: C57BL/6 BM was depleted of B220$^+$, CD3$^+$ and GR-1$^+$ cells and was expanded for 7 days with GM-CSF, IL-4 and Flt3L. A retroviral vector encoding luc and gfp was used for transduction. Gfp/luc$^+$ DCs were analyzed by FACS and injected i.v. at 4x10^6 DCs per animal into BALB/c mice that had received either allogeneic myeloablative BMT (BALB/c-mbl, n=5) or non-myeloablative (BALB/c-n/mbl, n=5) BMT of C57BL/6 BM donor mice 10 weeks prior. The *in vivo* trafficking of the gfp/luc+DCs was monitored by bioluminescent imaging (BLI). Tissues were examined for gfp$^+$ DCs using immunohistochemistry. Results: Expanded C57BL/6 DCs expressed CD80, CD86 and MHC II. After transduction, CD11c$^+$ gfp/luc$^+$ cells represented 20-27% of viable cells. After injection, gfp/luc$^+$ DCs were detectable in BALB/c-mbl and BALB/c-n/mbl mice over the entire observation period (BALB/c-mbl: 45d, BALB/c-n/mbl: 101d). Immediately after injection, a high bioluminescent signal (BLS) was detected in the pulmonary area. In BALB/c-mbl this signal decreased constantly until d10, while in the BALB/c-n/mbl the BLS decreased on d2 and remained stable until d23. In both groups on d2 and d7 BLSs were detected in the area of liver and spleen. Starting on d10 in BALB/c-mbl and on d23 in the BALB/c-n/mbl there was an increase of the BLS reaching a maximum in BALB/c-mbl on d35 and in BALB/c-n/mbl on d77. The increase of the BLS was seen in both groups in the area of the gut, the spleen and the thymus. These findings were confirmed by immunohistochemistry of gut and spleen sections which showed gfp$^+$CD11c$^+$ DCs. During the observation period no animal exhibited signs of GvHD. Conclusion: Here, we show that donor-derived, *ex vivo* expanded gfp/luc$^+$ DCs survive in hosts after allogeneic BMT. They migrate to thymus, spleen and gut, but mice develop no clinical signs of GVHD. The ability to visualize DC survival and trafficking in an allogeneic BMT setting will aid in the optimization of DC based treatment strategies.

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IMPROVING OUTCOMES OF HAPLOIDENTICAL TRANSPLANTS FOR ACUTE LEUKEMIA

Aversa, F.[1]; Terenzi, A.[1]; Ballanti, S.[1]; Felicini, R.[1]; Carotti, A.[1]; Falcinelli, F.[1]; Tabilio, A.[1]; Falzetti, F.[1]; Velardi, A.[1]; Santucci, A.[1]; Reisner, Y.[2]; Martelli, M.F.[1] 1. Hematology, Perugia, Perugia, Italy; 2. Weizmann Institute, Rehovot, Israel.

Our first report on 36 acute leukemia patients showed a mega-dose of T-depleted HSC is crucial factor in promoting engraftment across the HLA barriers. Modifications to our approach have led to remarkable progress. In 1995 fludarabine replaced cyclophosphamide in our TBI-based conditioning regimen and we started to select the CD34+ cells using the Ceprate system (44 patients). In 1999, we changed to the CliniMacs device and suspended post transplant G-CSF (65 patients). Population included 145 patients (age range: 2 - 62 years), 76 AML and 69 ALL, at high-risk of relapse because of disease status at transplant (27 bad-risk CR I, 48 CR  II, 70 in relapse). Disease status was